Confocal Biomicroscopy AIDS Early Detection of Wilson's Disease: A Case Report

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Abstract: Purpose: To report a case of asymptomatic Wilson's disease (WD) in which the identification of a Kayser-Fleischer (K-F) ring and its characterization by confocal biomicroscopy led to the diagnosis. **Methods**: Case report. Results: Confocal biomicroscopy showed clustered, highly reflective, and round foci in Descemet's membrane, which we believed to be depositions of copper in this patient with asymptomatic WD. **Conclusion**: WD is characterized by toxic copper accumulation that can result in irreversible organ damage, neurologic deficit, and even death. Patients concurrent WD and hepatitis B show aggregate manifestations and worse prognosis than those of patients with WD alone. Hence, early diagnosis and treatment of WD are important in populations with high hepatitis B prevalence. The presence of a K-F ring is a pathognomonic sign of WD but is often confused as a sign of another disease such as corneal dystrophy or toxic or metabolic disorder. Early use of confocal biomicroscopy prior to a traditional serum test, urine assay, and liver biopsy may provide a fast, accurate, and non-invasive method to detect WD and potentially save a patient's life.
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1. Introduction

Wilson's disease (WD) is an autosomal recessive inherited disease involving impairment of hepatic copper excretion. The resulting copper accumulation may cause dysfunction of multiple organs and can be life threatening. Traditionally, diagnosis of WD depends upon clinical hepatic and neurologic symptoms in addition to evidence of reduced serum ceruloplasmin and increased urinary copper levels and liver biopsy results. The presence of a Kayser-Fleischer (K-F) ring in the cornea is a pathognomonic feature of WD but can often be confused with signs of another disease such as corneal dystrophy or toxic or metabolic disorder. A delayed diagnosis of WD may lead to end-organ damage, while early treatment may improve patient outcomes and survival. Herein, we describe a case of asymptomatic WD in which a K-F ring was observed, leading to characterization via confocal biomicroscopy and a positive WD diagnosis.

2. Case report

A 20-year-old male patient with depressive disorder documented for 2 years consulted our ophthalmologic department regarding bothersome dryness and intermittent blurred vision in both eyes. A review of his previous medical history revealed chronic hepatitis B without regular follow up. Visual acuity was 20/20, with normal intraocular pressure, a brisk light reflex, and deep and clear anterior chambers in both eyes. A golden-brown arcus was found over the peripheral cornea of both eyes. Slit-lamp biomicroscopy showed deposition of a golden-brown pigment at the level of Descemet's membrane without abnormal findings in other layers (Figure 1A, 1B). Although the patient did not show any other signs, a WD-related K-F ring was highly suspected. Anterior segment optical coherence tomography of the cornea confirmed the finding of Descemet's membrane involvement (Figure 1C), and confocal microscopy showed the presence of highly reflective foci at the level of Descemet's membrane (Figure 1D). Subsequently, a systemic examination including a routine blood test, determination of serum ceruloplasmin level, liver function profile, 24-h urine copper assay, and liver biopsy were performed. The following results were obtained, confirming a diagnosis of WD: a low serum ceruloplasmin level (11 mg/dl), a high copper level in the 24-h urine assay (118 μg/24 h), and a positive liver biopsy. The patient then underwent penicillamine anti-copper therapy. Three years later, the patient showed no neurologic deficit, and the K-F ring gradually faded with a slight residual yellowish deposition.

3. Discussion

WD is an autosomal recessive inherited disease characterized by hepatolenticular degeneration due to a defect in copper transporting triphosphatase (ATP7B), and impairment of hepatic copper excretion. Toxic copper accumulation may result in dysfunction of multiple organs, including the liver, brain, and kidneys, and of the hematologic system. Symptoms usually appear by the age of 20 years, but some patients may not be diagnosed until they are over 40 years old. Although the appearance of a K-F ring around the cornea is a pathognomonic feature of WD, a positive diagnosis of WD depends upon clinical hepatic and neurologic symptoms, in addition to decreased serum ceruloplasmin level, increased urinary copper level, and hepatic copper accumulation indicated by biopsy. A delay in the diagnosis of WD can cause irreversible end-organ damage, while early treatment may improve patient outcomes and reduce mortality.

Ala et al. stated that WD is usually diagnosed on the basis of abnormal hepatic histology, which is viewed as the gold standard, an ophthalmologic finding of a K-F ring, and low serum ceruloplasmin level（1）. Although the appearance of a K-F ring in WD is typical in its manifestation of annular opacity involving only the peripheral Descemet's membrane, several case reports in the literature suggest consideration of the possibility of a pseudo-K-F ring associated with corneal dystrophy, toxic or metabolic disorder, primary biliary cirrhosis, chronic liver disease other than copper accumulation, or systemic malignancy（2,3,4,5,6）Although clinical manifestations and serologic findings can help clarify the diagnosis,[1] we believe that confocal biomicroscopy may aid in rapid and more accurate distinction of WD-specific corneal observations. Notably, K-F rings may have lower prevalence in younger patients with early-stage WD (5.6% of patients), even when poor liver function is observed, and have also been observed in the absence of other neurologic manifestations（7）. Confocal biomicroscopy reveals detailed in vivo pathology of the cornea, which is documented to aid precise diagnosis in recent ophthalmologic practice. We found clustered, highly reflective, and round foci in Descemet's membrane, which we believed to be depositions of copper in this WD patient. This confocal microscopic observation in our patient helped detect the underlying WD precisely and immediately. Therefore, penicillamine therapy could be initiated immediately and further possible organ damage could be prevented.

Taiwanese individuals with WD show special disease characteristics. Because 15~20% of the Taiwanese are hepatitis B carriers, those with concurrent WD and hepatitis B can show aggregate manifestations and worse prognosis than those of individuals with WD alone, and Chinese WD patients are particularly responsive to penicillamine therapy（8）. Hence, early diagnosis and treatment of WD are critical for Taiwanese individuals with hepatitis B. Although chronic hepatitis B is associated with hepatocellular carcinoma (HCC), some reports found a lower incidence of HCC in patients with WD and that copper may have a protective effect against this fatal disease（5,9）. However, more well-designed studies are needed to clarify the correlation between copper and HCC.

In conclusion, WD is characterized by toxic copper accumulation that results in irreversible organ damage, neurologic deficit, and even death. Early and accurate detection of this disease by using confocal biomicroscopy may provide a faster, more accurate, and non-invasive method for diagnosis, potentially saving patients' lives.

4. Figure legends

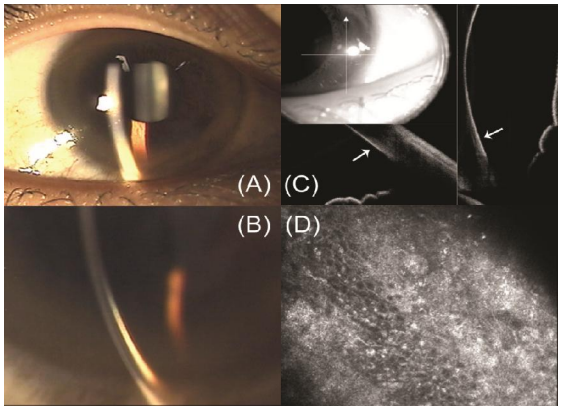

Figure 1. (A) Slit-Lamp biomicroscopy showed a peripheral golden-brown deposition under low magnification. (B) Slit-lamp biomicroscopy in high magnification showed the deposition to be at the level of Descemet's membrane. (C) Anterior segment optical coherence tomography shows high-density deposits in the peripheral cornea (arrow). (D) Confocal biomicroscopy at the level of Descemet's membrane shows multiple clustered, highly reflective and round foci consistent with copper deposition in Wilson's disease.

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